

The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

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| GSK Medicine: Diclofenac diethylammonium |
| Study Number: A2620383 |
| Title: A Proof of Principle Study to Investigate the Efficacy of a Medical Device and Topical Analgesic Combination for the Treatment of Pain and Performance Related Function in Osteoarthritis |
| Rationale: To determine whether the combination of topical diclofenac and a heat patch is more effective than the standard treatment topical diclofenac alone. |
| Phase: Not applicable |
| Study Period: 5th February 2008 to 12th June 2008 |
| Study Design: This was a proof of principle single centre study, single (assessor) blind, randomised, three way crossover, in subjects with osteoarthritis (OA) of the knee. Following a Screening Visit, eligible subjects underwent a washout period from their current OA medication of 7-14 days prior to the first Baseline Visit. All three treatment periods consisted of a Baseline Visit and a post-treatment visit which were separated by exactly 72 hours (hrs) of treatment. For each treatment period subjects applied the treatment two times a day for 72 hrs, each treatment application remained on the knee for approximately 8 hrs. There was a 7-10 day washout period between each treatment period. Subjects were provided with rescue medication (standard paracetamol) for use, if required, during the treatment and washout periods. Subjects completed the Western Ontario and McMaster's University (WOMAC) osteoarthritis index at all visits. The subject's pain, stiffness and difficulty to perform various activities were rated by subjects as per the WOMAC scale which is based on questionnaire. The responses were based on a 5-point Likert scale as detailed below: 0=None; 1=Mild; 2= Moderate; 3=Severe; 4=Extreme. Measurement of time to walk 20 meter (m), time to walk 40 m, stair climbing and subjective assessments of pain were made at all baseline and post-treatment visits. The subjects indicated their pain at that time using a pain rating scale. The pain rating was based on a 5-point Likert scale: 0 = None; 1 = Mild pain; 2 = Moderate pain; 3 = Severe pain; 4 = Extreme pain. A single plasma sample to determine diclofenac level was obtained at all post-treatment visits. |
| Centre: 1 in United Kingdom |
| Indication: Pain |
| Treatments: Test Product: Diclofenac gel (4 g of gel containing 1.16% diclofenac diethylammonium) with a heat patch Reference Products: 1. Diclofenac gel (4 g of gel containing 1.16% diclofenac diethylammonium) with a placebo heat patch (expelled of heat) 2. Placebo gel (4 g of gel) applied topically to the knee and covered with a heat patch |
| Objectives: Primary Objective: To compare the efficacy of 72 hrs treatment with topical diclofenac plus a heat patch to 72 hrs treatment with topical diclofenac plus a placebo patch on time to climb stairs and on pain following stair climbing Secondary Objectives: 1. To compare the efficacy of 72 hrs treatment of topical diclofenac plus a heat patch with 72 hrs treatment of placebo gel plus a heat patch on time to climb stairs and on pain following stair climbing. 2. To compare the efficacy of topical diclofenac plus heat patch with topical diclofenac plus placebo patch and to placebo gel plus heat patch on the following secondary endpoints: <ul style="list-style-type: none"> • Time to walk 20 m; • Time to walk 40 m; • Pain following walking 40 m; • Pain at rest; • WOMAC scores; • Mean consumption of rescue medication based on consumption per patient per treatment. |

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| Primary Outcome Endpoints: | |
| 1. Time to climb stairs on 72 hrs treatment of topical diclofenac plus a heat patch with 72 hrs treatment of topical diclofenac plus a placebo patch | |
| 2. Pain following stair climbing on 72 hours hrs treatment of topical diclofenac plus a heat patch with 72 hrs treatment of topical diclofenac plus a placebo patch | |
| Secondary Outcome Endpoints: | |
| 1. Time to climb stairs on 72 hrs treatment of topical diclofenac plus a heat patch with 72 hrs treatment of placebo gel plus a heat patch | |
| 2. Pain following stair climbing on 72 hrs treatment of topical diclofenac plus a heat patch with 72 hrs treatment of placebo gel plus a heat patch | |
| 3. Time to walk 20 m on treatment of topical diclofenac plus heat patch with topical diclofenac plus placebo patch and to placebo gel plus heat patch | |
| 4. Time to walk 40 m on treatment of topical diclofenac plus heat patch with topical diclofenac plus placebo patch and to placebo gel plus heat patch | |
| 5. Pain following walking 40 m on treatment of topical diclofenac plus heat patch with topical diclofenac plus placebo patch and to placebo gel plus heat patch | |
| 6. Pain at rest on treatment of topical diclofenac plus heat patch with topical diclofenac plus placebo patch and to placebo gel plus heat patch | |
| 7. WOMAC scores on treatment of topical diclofenac plus heat patch with topical diclofenac plus placebo patch and to placebo gel plus heat patch: | |
| 8. Mean consumption of rescue medication based on consumption per patient per treatment on treatment of topical diclofenac plus heat patch with topical diclofenac plus placebo patch and to placebo gel plus heat patch | |
| Statistical Methods: | |
| The primary efficacy analysis was a mixed model analysis of variance on time to climb stairs, followed by a multiple comparison t-test to compare topical diclofenac gel plus heat patch to topical diclofenac gel plus placebo patch. The fixed effects in the model were treatment and period; patient was a random effect. The multiple comparison t-tests were 2-sided, conducted at the 5% significance level. The same analysis was performed on the endpoint of pain following stair climbing. In the secondary efficacy analysis, another multiple comparison t-test was performed following the analysis of variance (ANOVAs) in the primary analysis, to compare topical diclofenac gel plus heat patch to placebo gel plus heat patch. The secondary parameters listed above were each analysed using the same model as in the primary analysis but the multiple comparisons following the ANOVA was a Dunnett's Test comparing topical diclofenac gel plus heat patch to each of topical diclofenac gel plus placebo patch and placebo gel plus heat patch. | |
| Study Population: | |
| Subject Disposition | |
| | Overall |
| Subjects Randomized, n | 69 |
| Subjects completed study, n | 63 |
| Subject did not complete the study, n | 6 |
| Reason for not completing the study, n | |
| Adverse Event | 0 |
| Lost To Follow-Up | 0 |
| Protocol Deviation | 2 |
| Withdrawal Of Consent | 0 |
| Other | 4 |
| Demographics (All Randomized Subjects) | |
| | Overall |
| N | 69 |
| Sex, n (%) | |
| Male: Female | 45 (65.2): 24 (34.8) |
| Mean Age, years (SD) | 67.59 (6.779) |
| Race, n (%) | |
| Caucasian | 68 (98.6) |
| Black | 1 (1.4) |
| Primary Outcome Results (Intent to Treat [ITT] population N=69): | |

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| Table 1: Time to climb stairs (seconds) on 72 hrs treatment of topical diclofenac plus a heat patch with 72 hrs treatment of topical diclofenac plus a placebo patch | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch |
| n | 68 | 65 |
| Mean (SD) | 26.82 (11.440) | 27.14 (12.582) |
| Median (Minimum [Min.]-Maximum [Max.]) | 24.00 (14.0-85.0) | 25.00 (13.0-98.0) |
| LS Mean | 26.73 | 27.12 |
| Treatment comparison | | |
| Topical Diclofenac +Heat Patch versus (vs.) Topical Diclofenac +Placebo Patch | | |
| Difference | -0.39 | |
| 95% CI | -1.86, 1.08 | |
| p-value | 0.8056 | |
| | | |
| Table 2: Pain (score on a scale) following stair climbing on 72 hrs treatment of topical diclofenac plus a heat patch with 72 hrs treatment of topical diclofenac plus a placebo patch | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch |
| n | 68 | 65 |
| Mean (SD) | 1.68 (0.984) | 1.78 (1.053) |
| Median (Min.-Max.) | 2.00 (0.0-4.0) | 2.00 (0.0-4.0) |
| LS Mean | 1.67 | 1.74 |
| Treatment comparison | | |
| Topical Diclofenac + Heat Patch vs. Topical Diclofenac + Placebo Patch | | |
| Difference | -0.07 | |
| 95% CI | -0.32, 0.18 | |
| p-value | 0.7895 | |
| | | |
| Secondary Outcome Results (ITT population N=69): | | |
| Table 3: Time (seconds) to climb stairs on 72 hrs treatment of topical diclofenac plus a heat patch with 72 hrs treatment of placebo gel plus a heat patch | | |
| Treatments | Topical Diclofenac+ Heat Patch | Placebo Gel+ Heat Patch |
| n | 68 | 65 |
| Mean (SD) | 26.82 (11.440) | 27.69 (12.180) |
| Median (Min.-Max.) | 24.00 (14.0- 85.0) | 24.00 (13.0-80.0) |
| LS Mean | 26.73 | 27.80 |
| Treatment comparison | | |
| Topical Diclofenac + Heat Patch vs. Placebo Gel + Heat Patch | | |
| Difference | -1.07 | |
| 95% CI | -2.44, 0.31 | |
| p-value | 0.1520 | |
| | | |
| Table 4: Pain (score on a scale) following stair climbing on 72 hrs treatment of topical diclofenac plus a heat patch with 72 hrs treatment of placebo gel plus a heat patch | | |
| Treatments | Topical Diclofenac+ Heat Patch | Placebo Gel+ Heat Patch |
| n | 68 | 65 |
| Mean (SD) | 1.68 (0.984) | 1.78 (1.008) |
| Median (Min.-Max.) | 2.00 (0.0-4.0) | 2.00 (0.0-4.0) |
| LS Mean | 1.67 | 1.74 |
| Treatment comparison | | |
| Topical Diclofenac + Heat Patch vs. Placebo Gel + Heat Patch | | |
| Difference | -0.07 | |
| 95% CI | -0.31, 0.17 | |
| p-value | 0.7231 | |

| Table 5: Time (seconds) to walk 20 m on treatment of topical diclofenac plus heat patch with topical diclofenac plus placebo patch and to placebo gel plus heat patch | | | |
|---|--------------------------------|-----------------------------------|-------------------------|
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 68 | 65 | 65 |
| Mean (SD) | 18.78 (6.279) | 18.83 (6.501) | 19.57 (7.351) |
| Median (Min.-Max.) | 18.00 (12.0-58.0) | 18.00 (12.0-53.0) | 18.00 (12.0-61.0) |
| LS Mean | 18.72 | 18.93 | 19.69 |
| Treatment comparison | | | |
| Topical Diclofenac + Heat Patch vs. Topical Diclofenac + Placebo Patch | | | |
| Difference | -0.22 | | |
| 95% CI | -1.03, 0.59 | | |
| p-value | 0.7697 | | |
| Topical Diclofenac + Heat Patch vs. Placebo Gel + Heat Patch | | | |
| Difference | -0.98 | | |
| 95% CI | -1.78, -0.17 | | |
| p-value | 0.0142 | | |
| | | | |
| Table 6: Time (seconds) to walk 40 m on treatment of topical diclofenac plus heat patch with topical diclofenac plus placebo patch and to placebo gel plus heat patch | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 68 | 65 | 65 |
| Mean (SD) | 38.57 (12.760) | 38.09 (11.051) | 39.91 (14.345) |
| Median (Min.-Max.) | 36.50 (21.0- 118.0) | 36.00 (25.0- 102.0) | 38.00 (25.0- 116.0) |
| LS Mean | 38.45 | 38.35 | 40.23 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | 0.10 | | |
| 95% CI | -1.28, 1.49 | | |
| p-value | 0.9796 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -1.78 | | |
| 95% CI | -3.17, -0.40 | | |
| p-value | 0.0087 | | |
| | | | |
| Table 7: Pain following walking 40 m on treatment of topical diclofenac plus heat patch with topical diclofenac plus placebo patch and to placebo gel plus heat patch | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 68 | 65 | 65 |
| Mean (SD) | 1.10 (1.010) | 1.17 (1.039) | 1.26 (1.079) |
| Median (Min.-Max.) | 1.00 (0.0- 4.0) | 1.00 (0.0- 4.0) | 1.00 (0.0- 4.0) |
| LS Mean | 1.09 | 1.12 | 1.22 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.03 | | |
| 95% CI | -0.29, 0.22 | | |
| p-value | 0.9451 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.13 | | |
| 95% CI | -0.38, 0.13 | | |
| p-value | 0.4276 | | |

| Table 8: Pain at rest on treatment of topical diclofenac plus heat patch with topical diclofenac plus placebo patch and to placebo gel plus heat patch | | | |
|--|--------------------------------|-----------------------------------|-------------------------|
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 68 | 65 | 65 |
| Mean (SD) | 0.59 (0.833) | 0.89 (0.954) | 0.89 (1.002) |
| Median (Min.-Max.) | 0.00 (0.0-3.0) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) |
| LS Mean | 0.58 | 0.87 | 0.87 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.28 | | |
| 95% CI | -0.53, -0.04 | | |
| p-value | 0.0185 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.28 | | |
| 95% CI | -0.53, -0.04 | | |
| p-value | 0.0176 | | |
| | | | |
| Table 9: WOMAC scores on treatment of topical diclofenac plus heat patch with topical diclofenac plus placebo patch and to placebo gel plus heat patch | | | |
| 1. Pain Walking On Flat Surface | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 68 | 65 | 64 |
| Mean (SD) | 1.32 (0.905) | 1.43 (0.829) | 1.38 (0.917) |
| Median (Min.-Max.) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) |
| LS Mean | 1.33 | 1.39 | 1.33 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.06 | | |
| 95% CI | -0.24, 0.12 | | |
| p-value | 0.6627 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | 0.00 | | |
| 95% CI | -0.18, 0.17 | | |
| p-value | 0.9980 | | |
| 2. Pain Going Up Or Down Stairs | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 66 | 65 | 64 |
| Mean (SD) | 1.89 (0.862) | 2.02 (0.780) | 1.97 (0.890) |
| Median (Min.-Max.) | 2.00 (0.0-3.0) | 2.00 (0.0-3.0) | 2.00 (0.0-4.0) |
| LS Mean | 1.89 | 2.00 | 1.95 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.10 | | |
| 95% CI | -0.36, 0.15 | | |
| p-value | 0.5709 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.06 | | |
| 95% CI | -0.32, 0.20 | | |
| p-value | 0.8248 | | |
| 3. Pain That Disturbs Your Sleep | | | |

| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
|--|-----------------------------------|--------------------------------------|----------------------------|
| n | 68 | 65 | 64 |
| Mean (SD) | 1.19 (1.011) | 1.45 (0.867) | 1.34 (0.996) |
| Median (Min.-Max.) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) | 1.00 (0.0-4.0) |
| LS Mean | 1.19 | 1.41 | 1.27 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.22 | | |
| 95% CI | -0.44, -0.01 | | |
| p-value | 0.0376 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.09 | | |
| 95% CI | -0.30, 0.12 | | |
| p-value | 0.5513 | | |
| 4. Pain Sitting Or Lying | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 68 | 65 | 64 |
| Mean (SD) | 1.25 (0.904) | 1.37 (0.928) | 1.23 (0.850) |
| Median (Min.-Max.) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) |
| LS Mean | 1.25 | 1.35 | 1.21 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.10 | | |
| 95% CI | -0.32, 0.12 | | |
| p-value | 0.4705 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | 0.04 | | |
| 95% CI | -0.18, 0.26 | | |
| p-value | 0.8935 | | |
| 5. Pain Standing Upright | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 68 | 65 | 63 |
| Mean (SD) | 1.43 (0.869) | 1.45 (0.771) | 1.46 (0.981) |
| Median (Min.-Max.) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) |
| LS Mean | 1.42 | 1.43 | 1.42 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | 0.00 | | |
| 95% CI | -0.20, 0.20 | | |
| p-value | 0.9989 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | 0.00 | | |
| 95% CI | -0.20, 0.20 | | |
| p-value | 0.9991 | | |
| 6. Severity of Stiffness after awake | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 65 | 63 | 61 |
| Mean (SD) | 1.60 (0.949) | 1.65 (0.883) | 1.67 (0.944) |
| Median (Min.-Max.) | 2.00 (0.0-3.0) | 2.00 (0.0-3.0) | 2.00 (0.0-4.0) |
| LS Mean | 1.61 | 1.66 | 1.67 |
| Treatment comparison | | | |

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| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.05 | | |
| 95% CI | -0.27, 0.16 | | |
| p-value | 0.8015 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.06 | | |
| 95% CI | -0.28, 0.16 | | |
| p-value | 0.7552 | | |
| 7. Severity Of Stiffness Later In Day | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 65 | 62 | 61 |
| Mean (SD) | 1.58 (0.768) | 1.61 (0.817) | 1.54 (0.886) |
| Median (Min.-Max.) | 2.00 (0.0-3.0) | 2.00 (0.0-3.0) | 2.00 (0.0-3.0) |
| LS Mean | 1.61 | 1.61 | 1.55 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | 0.01 | | |
| 95% CI | -0.20, 0.21 | | |
| p-value | 0.9970 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | 0.06 | | |
| 95% CI | -0.15, 0.27 | | |
| p-value | 0.7320 | | |
| 8. Difficulty In Descending Stairs | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 67 | 63 | 64 |
| Mean (SD) | 2.01 (0.945) | 2.05 (0.851) | 2.02 (0.882) |
| Median (Min.-Max.) | 2.00 (0.0-4.0) | 2.00 (0.0-3.0) | 2.00 (0.0-4.0) |
| LS Mean | 2.02 | 2.03 | 2.02 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.01 | | |
| 95% CI | -0.26, 0.24 | | |
| p-value | 0.9974 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | 0.00 | | |
| 95% CI | -0.25, 0.25 | | |
| p-value | 0.9999 | | |
| 9. Difficulty In Ascending Stairs | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 67 | 62 | 64 |
| Mean (SD) | 1.96 (0.928) | 2.13 (0.799) | 2.00 (0.836) |
| Median (Min.-Max.) | 2.00 (0.0-4.0) | 2.00 (0.0-3.0) | 2.00 (0.0-3.0) |
| LS Mean | 1.95 | 2.12 | 1.99 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.16 | | |
| 95% CI | -0.39, 0.07 | | |
| p-value | 0.1946 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.04 | | |
| 95% CI | -0.26, 0.19 | | |

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|--|--------------------------------|-----------------------------------|-------------------------|
| p-value | 0.9039 | | |
| 10. Difficulty In Rising From Sitting | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 67 | 63 | 64 |
| Mean (SD) | 1.63 (0.902) | 1.62 (0.812) | 1.67 (0.944) |
| Median (Min.-Max.) | 2.00 (0.0-3.0) | 2.00 (0.0-3.0) | 2.00 (0.0-4.0) |
| LS Mean | 1.64 | 1.61 | 1.67 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | 0.03 | | |
| 95% CI | -0.19, 0.24 | | |
| p-value | 0.9492 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.03 | | |
| 95% CI | -0.24, 0.18 | | |
| p-value | 0.9291 | | |
| 11. Difficulty In Standing | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 67 | 63 | 64 |
| Mean (SD) | 1.39 (0.920) | 1.43 (0.817) | 1.45 (0.942) |
| Median (Min.-Max.) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) |
| LS Mean | 1.40 | 1.43 | 1.45 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.03 | | |
| 95% CI | -0.22, 0.17 | | |
| p-value | 0.9288 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.04 | | |
| 95% CI | -0.24, 0.15 | | |
| p-value | 0.8300 | | |
| 12. Difficulty In Bending To Floor | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 67 | 63 | 64 |
| Mean (SD) | 1.91 (0.917) | 1.97 (0.967) | 1.91 (0.868) |
| Median (Min.-Max.) | 2.00 (0.0-3.0) | 2.00 (0.0-4.0) | 2.00 (0.0-3.0) |
| LS Mean | 1.92 | 1.95 | 1.90 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.03 | | |
| 95% CI | -0.23, 0.18 | | |
| p-value | 0.9338 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | 0.03 | | |
| 95% CI | -0.18, 0.23 | | |
| p-value | 0.9448 | | |
| 13. Difficulty Walking On Flat Surface | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 67 | 63 | 64 |
| Mean (SD) | 1.33 (0.927) | 1.37 (0.867) | 1.36 (0.949) |
| Median (Min.-Max.) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) | 1.00 (0.0-4.0) |

| | | | |
|--|--------------------------------|-----------------------------------|-------------------------|
| LS Mean | 1.34 | 1.35 | 1.33 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | 0.00 | | |
| 95% CI | -0.20, 0.20 | | |
| p-value | 0.9992 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | 0.01 | | |
| 95% CI | -0.18, 0.21 | | |
| p-value | 0.9855 | | |
| 14. Difficulty In Getting In/Out Of Car | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 64 | 64 | 65 |
| Mean (SD) | 1.77 (0.868) | 1.84 (0.801) | 1.82 (0.917) |
| Median (Min.-Max.) | 2.00 (0.0-3.0) | 2.00 (0.0-3.0) | 2.00 (0.0-4.0) |
| LS Mean | 1.77 | 1.83 | 1.80 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.06 | | |
| 95% CI | -0.26, 0.15 | | |
| p-value | 0.7703 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.03 | | |
| 95% CI | -0.23, 0.17 | | |
| p-value | 0.9257 | | |
| 15. Difficulty In Going Shopping | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 61 | 62 | 63 |
| Mean (SD) | 1.54 (0.867) | 1.73 (0.813) | 1.63 (1.036) |
| Median (Min.-Max.) | 2.00 (0.0-3.0) | 2.00 (0.0-3.0) | 2.00 (0.0-4.0) |
| LS Mean | 1.57 | 1.67 | 1.61 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.10 | | |
| 95% CI | -0.31, 0.11 | | |
| p-value | 0.4716 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.04 | | |
| 95% CI | -0.25, 0.17 | | |
| p-value | 0.8916 | | |
| 16. Difficulty In Putting Socks/Tights | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 64 | 63 | 64 |
| Mean (SD) | 1.52 (0.943) | 1.54 (0.895) | 1.53 (0.908) |
| Median (Min.-Max.) | 1.00 (0.0-3.0) | 2.00 (0.0-3.0) | 1.00 (0.0-4.0) |
| LS Mean | 1.52 | 1.51 | 1.52 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | 0.00 | | |
| 95% CI | -0.19, 0.20 | | |
| p-value | 0.9977 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |

| | | | |
|--|--------------------------------|-----------------------------------|-------------------------|
| Difference | 0.00 | | |
| 95% CI | -0.20, 0.19 | | |
| p-value | 0.9992 | | |
| 17. Difficulty In Rising From Bed | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 64 | 64 | 65 |
| Mean (SD) | 1.53 (1.023) | 1.56 (0.924) | 1.58 (0.983) |
| Median (Min.-Max.) | 1.50 (0.0-4.0) | 2.00 (0.0-3.0) | 2.00 (0.0-4.0) |
| LS Mean | 1.53 | 1.52 | 1.57 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | 0.01 | | |
| 95% CI | -0.22, 0.24 | | |
| p-value | 0.9935 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.04 | | |
| 95% CI | -0.27, 0.18 | | |
| p-value | 0.8673 | | |
| 18. Difficulty in taking off socks | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 63 | 63 | 64 |
| Mean (SD) | 1.52 (0.965) | 1.48 (0.965) | 1.53 (0.959) |
| Median (Min.-Max.) | 1.00 (0.0-3.0) | 2.00 (0.0-3.0) | 1.50 (0.0-4.0) |
| LS Mean | 1.52 | 1.47 | 1.53 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | 0.05 | | |
| 95% CI | -0.15, 0.25 | | |
| p-value | 0.7927 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.01 | | |
| 95% CI | -0.20, 0.19 | | |
| p-value | 0.9924 | | |
| 19. Difficulty In Lying In Bed | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 64 | 64 | 65 |
| Mean (SD) | 1.16 (0.912) | 1.31 (0.924) | 1.31 (0.983) |
| Median (Min.-Max.) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) |
| LS Mean | 1.16 | 1.26 | 1.27 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.10 | | |
| 95% CI | -0.30, 0.10 | | |
| p-value | 0.4287 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.11 | | |
| 95% CI | -0.31, 0.09 | | |
| p-value | 0.3519 | | |
| 20. Difficulty In Getting In/Out Of Bath | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 57 | 54 | 53 |

| | | | |
|--|-----------------------------------|--------------------------------------|----------------------------|
| Mean (SD) | 1.89 (0.976) | 2.02 (0.921) | 1.87 (1.057) |
| Median (Min.-Max.) | 2.00 (0.0-4.0) | 2.00 (0.0-4.0) | 2.00 (0.0-4.0) |
| LS Mean | 1.93 | 2.04 | 1.88 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.11 | | |
| 95% CI | -0.33, 0.11 | | |
| p-value | 0.4257 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | 0.04 | | |
| 95% CI | -0.18, 0.26 | | |
| p-value | 0.8759 | | |
| 21. Difficulty In Sitting | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 68 | 64 | 63 |
| Mean (SD) | 1.25 (0.870) | 1.36 (0.897) | 1.32 (0.981) |
| Median (Min.-Max.) | 1.00 (0.0-3.0) | 1.00 (0.0-3.0) | 1.00 (0.0-4.0) |
| LS Mean | 1.26 | 1.34 | 1.30 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.09 | | |
| 95% CI | -0.26, 0.09 | | |
| p-value | 0.4395 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.05 | | |
| 95% CI | -0.23, 0.13 | | |
| p-value | 0.7605 | | |
| 22. Difficulty In Getting On/Off Toilet | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 68 | 65 | 63 |
| Mean (SD) | 1.47 (0.889) | 1.55 (0.830) | 1.59 (0.927) |
| Median (Min.-Max.) | 1.50 (0.0-3.0) | 2.00 (0.0-3.0) | 2.00 (0.0-4.0) |
| LS Mean | 1.47 | 1.54 | 1.59 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.07 | | |
| 95% CI | -0.27, 0.14 | | |
| p-value | 0.6733 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.11 | | |
| 95% CI | -0.32, 0.09 | | |
| p-value | 0.3646 | | |
| 23. Difficulty In Heavy Domestic Duty | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 64 | 64 | 63 |
| Mean (SD) | 2.14 (0.814) | 2.30 (0.749) | 2.19 (0.895) |
| Median (Min.-Max.) | 2.00 (0.0-3.0) | 2.00 (1.0-3.0) | 2.00 (0.0-4.0) |
| LS Mean | 2.18 | 2.26 | 2.19 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.08 | | |
| 95% CI | -0.27, 0.10 | | |

| | | | |
|---|--------------------------------|-----------------------------------|-------------------------|
| p-value | 0.5031 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.01 | | |
| 95% CI | -0.20, 0.18 | | |
| p-value | 0.9948 | | |
| 24. Difficulty In Light Domestic Duty | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 68 | 65 | 64 |
| Mean (SD) | 1.34 (0.874) | 1.46 (0.772) | 1.48 (0.854) |
| Median (Min.-Max.) | 1.00 (0.0-3.0) | 2.00 (0.0-3.0) | 1.00 (0.0-3.0) |
| LS Mean | 1.34 | 1.43 | 1.46 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.08 | | |
| 95% CI | -0.29, 0.13 | | |
| p-value | 0.5741 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.12 | | |
| 95% CI | -0.33, 0.09 | | |
| p-value | 0.3483 | | |
| | | | |
| Table 10: Mean consumption of rescue medication based on consumption per patient per treatment on treatment of topical diclofenac plus heat patch with topical diclofenac plus placebo patch and to placebo gel plus heat patch | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| n | 68 | 65 | 65 |
| Mean (SD) | 3.82 (5.148) | 4.12 (4.897) | 4.37 (7.331) |
| Median (Min.-Max.) | 0.00 (0.0- 16.0) | 2.00 (0.0- 16.0) | 0.00 (0.0- 48.0) |
| LS Mean | 3.86 | 3.93 | 4.30 |
| Treatment comparison | | | |
| Topical Diclofenac +Heat Patch vs. Topical Diclofenac+ Placebo Patch | | | |
| Difference | -0.07 | | |
| 95% CI | -1.37, 1.23 | | |
| p-value | 0.9889 | | |
| Topical Diclofenac +Heat Patch vs. Placebo Gel+ Heat Patch | | | |
| Difference | -0.44 | | |
| 95% CI | -1.73, 0.86 | | |
| p-value | 0.6697 | | |
| Safety Results (Safety population, N=69): | | | |
| Table 11: Number of Subjects With Treatment Emergent Adverse Events (AEs) | | | |
| Treatments | Topical Diclofenac+ Heat Patch | Topical Diclofenac+ Placebo Patch | Placebo Gel+ Heat Patch |
| N | 68 | 65 | 65 |
| Number of subjects with at least one AE, n (%) | 5 (7.4) | 14 (21.5) | 11 (16.9) |
| Musculoskeletal And Connective Tissue Disorders | | | |
| Joint Swelling | 0 | 3 (4.6) | 2 (3.1) |
| Osteoarthritis | 0 | 1 (1.5) | 1 (1.5) |
| Arthralgia | 0 | 1 (1.5) | 0 |
| Back Pain | 0 | 1 (1.5) | 0 |
| Groin Pain | 0 | 0 | 1 (1.5) |
| Pain In Extremity | 0 | 0 | 1 (1.5) |

| | | | |
|---|---------|---------|---------|
| Infections And Infestations | | | |
| Upper Respiratory Tract Infection | 1 (1.5) | 1 (1.5) | 1 (1.5) |
| Localised Infection | 0 | 1 (1.5) | 1 (1.5) |
| Skin And Subcutaneous Tissue Disorders | | | |
| Erythema | 2 (2.9) | 0 | 0 |
| Pruritus | 0 | 0 | 2 (3.1) |
| Skin Induration | 0 | 1 (1.5) | 0 |
| Gastrointestinal Disorders | | | |
| Nausea | 1 (1.5) | 1 (1.5) | 0 |
| Diarrhoea | 1 (1.5) | 0 | 0 |
| Dyspepsia | 0 | 0 | 1 (1.5) |
| General Disorders And Administration Site Conditions | | | |
| Fatigue | 0 | 2 (3.1) | 0 |
| Discomfort | 0 | 1 (1.5) | 0 |
| Feeling Hot | 0 | 1 (1.5) | 0 |
| Nervous System Disorders | | | |
| Headache | 0 | 2 (3.1) | 1 (1.5) |
| Dizziness | 0 | 0 | 1 (1.5) |
| Respiratory, Thoracic And Mediastinal Disorders | | | |
| Oropharyngeal Pain | 0 | 0 | 1 (1.5) |
| Vascular Disorders | | | |
| Hypertension | 1 (1.5) | 0 | 0 |
| Serious Adverse Events (SAEs) - On-Therapy | | | |
| No SAE was reported. | | | |